Modern Concepts of Cardiovascular Disease

Published monthly by the AMERICAN HEART ASSOCIATION

44 EAST 23RD STREET, NEW YORK 10, N. Y.

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Vol. XXIV **JULY, 1955** **No. 7**

THE LOW SALT SYNDROME*

"The low salt syndrome"[1] is not only a therapeutic problem, it is also a problem in semantics. Although in the chemical sense the word "salt" has a much wider connotation, it is commonly used to mean sodium chloride. The "low salt syndrome" must be further partitioned for clinical purposes into those situations characterized by low concentrations of sodium in the extracellular fluid (hyponatremia), low concentrations of chloride (hypochloremia), and situations in which concentrations of both ions are equally depressed. We must, however, further qualify our description by noting that a patient may be depleted of sodium chloride with normal plasma concentrations for both of these ions under circumstances where both water and sodium chloride have been lost in the same proportion. When this occurs, total body stores of sodium chloride may be depleted, but this may not be apparent by sampling the concentrations of the plasma since no change in *concentration* may have occurred. Thus, the rate and the proportion of the losses will determine the chemical and clinical pattern. The situation is further complicated by the role that other electrolytes, notably potassium, may play in the production and modification of this syndrome, as well as by the effect of metabolic disturbances in changing the usual distribution of sodium between cell and extracellular fluid. We may classify these various "low salt syndromes" as follows:

I. Patients in whom the *serum concentrations of sodium and chloride are proportionally and equally decreased.* This may occur when:

A. Sodium chloride losses exceed sodium chloride intake by reason of (1) excess salt losses, (2) drastic restriction of salt intake, and (3) a combination of excessive salt restriction and loss.

B. Dilution occurs by reason of excess water retention due to (1) excess water intake, (2) inadequate renal losses of water, and (3) a combination of both the above mentioned situations.

II. Those patients in whom *hypochloremia* is predominant (serum chloride concentrations depressed out of proportion to those of sodium). This may occur by reason of:

A. Excess chloride loss (profuse mercurial diuresis, vomiting).

B. Potassium depletion which may enhance or precipitate a clinical syndrome characterized by hypochloremic alkalosis.

III. Patients in whom *hyponatremia* is predominant, (sodium concentration is depressed beyond that of chloride). This may occur as a result of:

A. The administration of agents which specifically effect sodium excretion by the renal tubule (Diamox®) or the gastrointestinal tract (the cation exchange resins).

B. Losses from the lower gastrointestinal tract (diarrhea, intestinal drainage) which contain a higher proportion of sodium than of chloride.

C. The "adaptation syndrome", a metabolic disturbance common to chronic disease, anoxia, malnutrition in which the concentration of sodium in the extracellular fluid (and thus its tonicity) is altered as a result of a generalized metabolic defect.

Depression of both sodium and chloride concentration.

1. *Excess loss.* The true "low salt syndrome" may be seen under a variety of circumstances, all characterized by large losses of sodium chloride in excess of those of water. Many of these situations result directly from therapeutic maneuvers and may be precipitated or aggravated by drastic sodium restriction[2] with or without the administration of excess water. They include:

A. Frequent mercurial diureses.

B. Profuse sweating, replaced by salt-free liquids.

C. Repeated mechanical removal of large volumes of salt-containing fluids with replacement of water only (for example, paracentesis[3], thoracentesis, Southey tube drainage, and intestinal and gastric drainage).

D. Excess sodium wasting from the kidneys

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due either to impaired renal function or to deficiency of adrenal cortical hormones.

It is obvious that several of these situations may operate simultaneously. Under these circumstances the classical clinical signs of dehydration may be prominent. They include drowsiness, nausea, apathy, weakness, decreased skin turgor, and hypotension. These may progress to oliguria and nitrogen retention. It should be emphasized that it is not the decreased *concentration* of sodium and chloride per se that impairs renal function, but the over-all deficit of electrolyte and water operating through the resultant decrease in extracellular fluid volume. The hematocrit may be elevated, and serum total protein increased. Both serum sodium and chloride are proportionately depressed. (In the nephrotic patient high serum lipid values may result in falsely low serum sodium values, since the displacement of serum water by lipid may result in error in calculating the aqueous concentration of sodium).

The treatment is repair of the defect by a solution containing sodium and chloride in excess of water, that is, by a hypertonic solution. Where ever possible this should be done by mouth, employing ordinary dietary salt. The use of bouillion (containing 3½ gm of salt per cube) is to be preferred to enteric coated sodium chloride tablets, because of the greater certainty of absorption. Hypertonic salt solutions (3% or 5% saline) may be given by vein but this should be done with caution. The expansion of extracellular fluid and plasma volume by the rapid infusion of hypertonic salt solutions may result in pulmonary edema. Hypertonic sodium solutions are effective potassium antagonists, and patients with sodium depletion are also likely candidates for potassium depletion. Under such circumstances the infusion of hypertonic sodium solutions may aggravate the physiologic effect of potassium depletion. In the digitalized patient this may result in the production of digitalis intoxication and arrhythmias.

Where the serum sodium concentration is 120 mEq/L, the theoretical sodium deficit may be calculated from the formula:

(Normal concentration) 140 mEq/L—(actual concentration) 120 mEq/L = deficit = 20 mEq/L.

20 mEq/L x total body water (liters) = total sodium deficit in mEq.

One third of this calculated deficit should be infused slowly (1 gm of sodium chloride = 17 mEq of sodium).

Where sodium chloride depletion has been correctly diagnosed, clinical improvement will become manifest within a few hours, the serum sodium and chloride values will rise, urine volume and blood pressure will improve. Frequently one-half to one-third of the calculated dose may be all that is required to bring about complete clinical improvement and normal serum sodium and chloride concentrations. Under these circumstances it is probable that the infusion of the hypertonic salt solution withdraws water from the intracellular compartment. This water is then excreted by the kidneys whose function has been improved by increase in extracellular fluid volume. The resultant water loss increases the concentration of solute throughout body fluids generally and this is manifested by an increase in the serum sodium and chloride values.

2. *Dilution.* Decrease in sodium and chloride concentrations as a result of excess retention of water may be a factor particularly in postoperative cardiac patients, or in those whom excess water has been administered in an ill-advised attempt at therapy. This phenomenon is common in patients with renal failure and particularly so in the anuric patient. Under these circumstances the treatment of choice in repairing the concentration defect is not the administration of hypertonic sodium, but drastic restriction of water.

Hypochloremia

1. *Chloride losses which exceed those of sodium.* This syndrome is common as a result of prolonged vomiting. In the cardiac patient it is particularly frequent in those with a history of prolonged and effective mercurial diureses since the mercurial diuretics commonly produce urinary chloride/sodium ratios which exceed unity. Such a patient may respond well to diuretic therapy and then become refractory. Signs and symptoms of dehydration listed previously may be present. Characteristically the serum bicarbonate (as measured by carbon dioxide combining power or content) is elevated and the serum chloride concentration low. The treatment of choice under these circumstances is repair of general hydration. Administration of ammonium chloride is indicated to replenish depleted chloride stores. This may be given in doses of 3-4 gm daily by mouth in solution or gelatin capsules in preference to the poorly absorbed enteric coated capsules. Rarely it may be necessary to administer a 2% solution of ammonium chloride by vein. This should be given at a rate no greater than 200 cc in a four-hour period and should never be employed in the presence of impending liver disease.

2. Potassium depletion alone may precipitate or aggravate the syndrome of hypochloremic alkalosis. Where potassium deficits have occurred as in prolonged diarrhea, potassium chloride should be added to the replacement therapy. Rarely mercurial diuretics and more frequently Diamox® may cause prolonged and excessive urinary potassium wasting.

Hyponatremia (depression of serum sodium concentrations disproportionate to those of chloride).

The signs and symptoms may be similar to

those of other forms of dehydration. In addition, there may be a history of:

1. The prolonged use of Diamox®, or the cation exchange resins.

2. Diarrhea.

Serum sodium concentration is lowered proportionately more than that of serum chloride. Serum bicarbonate is decreased and in extreme instances profound acidosis with marked Kussmaul respiration may be present. Therapy is to discontinue the offending drug. If no total dehydration exists, the relative hyperchloremia may be corrected by the use of the mercurial diuretics. Where dehydration is present, however, correction of the specific sodium deficit must be accomplished by the use of a sodium salt with an anion which is metabolized (sodium bicarbonate or sodium lactate). The possibility of concomitant potassium deficits must also be remembered.

3. Under varying disease conditions with metabolic abnormalties, total body sodium may be normal or even increased although the serum concentration is low. It is probable that metabolic abnormalities within the cell result in a new setting for the tonicity of body fluids. It is possible that disturbance in cellular metabolism due to chronic disease, anoxia, or malnutrition may interfere with energy supplying mechanisms which in turn effect changes in the tonicity of body fluids with resultant transfers of both sodium and water, cellular and extracellular fluid. The low serum sodium values observed under these conditions can be rectified only by ameliorating the underlying metabolic difficulty and not by the addition of excess sodium to the body fluids. The hyponatremia here is a result rather than a cause of underlying disease. This type of low sodium syndrome may not be easily recognized clinically. It may be represented by the postoperative patient who is doing well in all respects but whose serum sodium is low. It may be seen in patients under chronic stress or in those with long-standing wasting illnesses and cachexia. Chronic congestive heart failure, terminal carcinoma, and severe tuberculosis are examples. Such patients may have no signs or symptoms referrable to electrolyte disturbance despite the fact that they are conserving urinary sodium and have hyponatremia. The nature of this particular syndrome is well delineated by the typical clinical course of the patient with severe congestive failure who undergoes successful corrective mitral valvulotomy. Under the stress of operation such a patient may show a sudden and marked drop in serum sodium for the first few days in spite of sodium retention, and a marked increase in total body sodium stores.[4] However, as cardiac dynamics improve, urinary sodium losses increase and a marked negative balance for sodium may be obtained at the same time that the serum concentrations spontaneously rise to normal values. Obviously the initial defect in this instance was not sodium depletion and no good purpose would have been served by infusing hypertonic salt solutions in an attempt to correct hyponatremia during the earlier postoperative period. There is recent evidence[5] that under these circumstances water retention may contribute a major share to dilution and thus hyponatremia. Under these circumstances therapy should be water restriction. Frequently it may be difficult to rule out sodium depletion as a major or contributory cause in hyponatremia even under the circumstances listed above. When in doubt, a cautious trial of sodium therapy may be made employing the safeguards listed above. Failure to respond clinically or with improved serum concentrations should contraindicate further sodium therapy.

Summary

The "low salt syndrome" is not a single entity but for proper understanding and therapy must be divided in to the following clinical entities:

1. Those situations in which concentrations of both sodium and chloride are equally depressed.

2. Those situations in which the concentration of sodium is primarily depressed (hyponatremia).

3. Those situations in which the concentration of chloride is predominantly depressed (hypochloremia).

The pathogenesis and principles of treatment for each of these situations are discussed. A fourth clinical situation is described in which hyponatremia (and to a lesser extent, hypochloremia) may represent an adaptation to more fundamental metabolic disorders. Repair of the concentration defect under these circumstances cannot be accomplished by electrolyte therapy alone, but must depend upon the reversibility of the underlying metabolic defect.

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